

REMARKS

Claims 1-3, 5-10, 12 and 14-19 are pending. Applicants herewith amend claims 17, 18 and 19 in order to correct an obvious grammatical error. Applicants add new claims 20 and 21. No new matter is added with this amendment. Support for new claims 20 and 21 can be found in the specification, *inter alia*, at page 5, lines 17-21 and page 6, lines 15-28. The Office Action is discussed below:

Claim Rejection under USC § 103

On page 2 of the Office Action, the examiner maintains the rejection of claims 1-3, 5-10, 12, and 14-19 as being obvious over Ohtsuka *et al.* (US 6,372,735) in view of Hancock *et al.* (*Pharma Res.*, Vol. 17, No. 4, 2000). According to the Examiner, Ohtsuka *et al.* teaches the compound of Example 20 (col. 42, line 15 to col. 43 line 34), which differs from the claimed compound by being in crystalline, rather than amorphous form. The Examiner cites Hancock *et al.* for allegedly teaching that amorphous compounds are more soluble than their crystalline counterparts and concludes that one skilled in the art would be motivated to convert crystalline pharmaceuticals into their amorphous counterparts and arrive at the claimed invention.

Applicants respectfully disagree for the legal reasons already of record, which are incorporated by reference here. However, in further response, applicants attach the Rule 132 declaration of Toyoaki Ishikura, who used four different ways to convert the crystalline compound of Example 20 into amorphous form. These four methods, lyophilization, mechanochemical conversion by an extruder, solvent distilling-off method and milling, were all unsuccessful in converting crystalline Compound A to an amorphous form. Although comminution by milling machine gave amorphous Compound A, the compound did not remain in this amorphous form and crystallized after storage at 60 degrees centigrade for two weeks. Because the amorphous state of this product could not be maintained, this product could not be used in a pharmaceutical. Applicants assert that the methods used by Dr. Ishikura in the study described in his declaration were routine, well –accepted methods that would have been used by the skilled artisan in the field of the invention. The present specification

describes such methods at page 2, lines 19 to page 3, line 3.

Aside from Dr. Ishikura's latest attestations in the Rule 132 declaration, Applicants describe the difficulty in converting the crystalline Compound A to an amorphous form at pages 2 to 3 of the specification and explain why traditional means for converting Compound A had not been successful. In fact, it was surprising to arrive at the present invention in view of the difficulties described in the specification and in the present declaration of Dr. Ishikura.

At best, the Examiner's rejection over Ohtsuka and Hancock amounts to an "obviousness to try" argument. But, "obvious to try" is not the proper standard for assessing obviousness in the United States. The cited art must guide the skilled artisan toward the invention. Neither cited reference suggests any of the difficulties applicants overcame and, therefore, neither reference provides guidance as to how to overcome such difficulties. In view of these deficiencies in the cited references and the evidence provided in Dr. Ishikura's declaration, applicants respectfully request Examiner Kifle to reconsider and withdraw the rejection for obviousness.


REQUEST

In view of above remarks, applicants respectfully submit that claims 1-3, 5-10, 12, 14-19 and 20 and 21 are allowable, and respectfully request favorable consideration to that effect. The Examiner is invited to contact the undersigned at (202) 912-2142 should there be any questions.

Respectfully submitted,

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Date

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